This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150.

See reverse side for additional information.

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 48-R-0002 **CUSTOMER NO.** 1459

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY *(Name and Address, as registered with USDA, include Zip Code)*

UNIVERSITY OF KANSAS
ANIMAL CARE UNIT
B054 MALOTT HALL
LAWRENCE, KS 66045

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS *(sites)*

UNIVERSITY OF KANSAS ANIMAL CARE UNIT
LAWRENCE, KS 66045

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY *(Attach additional sheets if necessary or use APHIS FORM 7023A)*

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic,analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs		4			4
5. Cats					
6. Guinea Pigs					
7. Hamsters					
8. Rabbits			81	10	91
9. Non-Human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). **A summary of all the exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

SIGNATURE OF C.E.O. OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		10/02/2006

APHIS FORM 7023 (AUG 91) (Replaces VS FORM 18-23 (Oct 88), which is obsolete) **PART 1 - HEADQUARTERS**

OCT 10 2006

APHIS Form 7023 Column E Explanation

This form is intended as an aid to completing the APHIS Form 7023 Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

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1. Registration Number: 48-R-0002

2/3. Species (common name) & Number of animals used in this study:

Rabbits (10)

4. Explain the procedure producing pain and/or distress.

Please see the response for Question #5.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Response for Question #4 & #5:

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: N/A CFR:

1. Registration Number: 48-R-0002 / 1459

2/3. Species (common name) & Number of animals used in this study:

Rabbits (10)

4. Explain the procedure producing pain and/or distress.

Please see the response for Question #5.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

Response for Question #4 & #5: One study on rabbits involves the injection of LPS (endotoxin) a model of sepsis. While this is not painful it may potentially result in distress to the animals. The experiment is intended to study the treatment of sepsis with a drug, AK-262. The major objective of this project is to confirm results pertaining to protective effects of the compound that was designed to bind to bacterial lipopolysaccharides (LPS) and neutralize them in a panel of vitro assays as well as in a murine model of LPS-induced septic shock. The results we have obtained so far indicate that this compound is highly efficacious, and yet is without discernable toxicity. Extensive in vitro studies such as inhibition of LPS-stimulated nitric oxide production (murine J774 cells), cytokine inhibition (TNf-alpha, IL-1 beta, IL-6, IL-8; in human blood ex vivo), inhibition of LPS-stimulated p38 MAP kinase (human neutrophils), inhibition of LPS-stimulated NF-kappa-B (human HEK-239 cells) all indicate excellent LPS-neutralizing activity of the compound. Furthermore, extensive in vivo data (CF-1 mouse) confirm that the anti-lipopolysaccharide activity of AK-262 is highly effective. We need to demonstrate that AK-262 effective in an animal model that does not need D-galactosamine sensitization to the effects of lipopolysaccharide? Animals that are highly sensitive to lipopolysaccharide are humans, rabbits, and horses. Mice are relatively resistant. Mice, therefore, need to be sensitized to the lethal effects of the toxin by administering D-galactosamine. Rabbits are a feasible model in this context to obtain confirmatory pre-clinical data. In animals receiving the test compound (AK-262), it is possible that some animals may become sick and may therefore need to be euthanized before the end of the one-week observation period. All animals will be monitored twice daily for significant clinical signs including listlessness and or lethargy, dyspnea, altered consciousness, seizures, anorexia and diarrhea. Any animal that becomes excessively ill will be euthanized as described above, after consultation with the attending veterinarian.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: N/A CFR:

Approval Status:
Approved/Disapproved By:
Date:

Disapproved Reason:

Customer Number: 1459
Certificate Number: 48-R-0002

Re: November 30th correspondence to KU Lawrence

Rabbits (10)
Briefly explain how the use of pain and/or distress relieving drugs would interfere with the objectivity of the study.

We use non-lethal doses of lipopolysaccharide that induces a measurable pyrogenic [temperature] response (0.6-1 deg. Celsius). The pyrogenic response in rabbits is a test that is commonly used in the validation of almost any pharmaceutical preparation for parenteral use. The use of any concomittant NSAIDs or antipyretics will obtund the pyrogenic response, thus completely invalidating the assay. This is the reason that we do not propose to use analgesics or antipyretics.

Please let us know if further information is needed to process our annual report.